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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,273	07/24/2006	Rolf Berge	966917.00013	6395

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EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	PAPER NUMBER
1645	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,273	BERGE ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-50* is/are pending in the application.

4a) Of the above claim(s) *24-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-23 and 44-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 3/24/09 has been entered into the record. Claims 1-21 have been cancelled. Claims 22-50 are pending in the application. Claims 24-43 are withdrawn. Claims 22-23 and 44-50 are under examination.

Rejections Withdrawn

The rejection of claims 22-23 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the amendment to the claims.

The rejection of claims 22-23 under 35 U.S.C. 102(b) as being clearly anticipated by Pang et al. (WO 02/34273 A1 May 2, 2002) is withdrawn in view of the amendment to the claims.

The rejection of claim 22 under 35 U.S.C. 102(b) as being clearly anticipated by Pedraglio et al (EP 0861905 A2 Sept. 2 1998) is withdrawn in view of the amendment to the claims.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-23 and 44-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing plasma homocysteine, reducing triacylglycerols in the liver, reducing the activity of Acyl-CoA:cholesterol acyltransferase (ACAT), increasing mitochondrial β-oxidation and changing the fatty acyl profile in an animal in need thereof comprising administering to said animal a pharmaceutical or nutritional composition comprising a single cell protein material, wherein the single cell protein material is harvested from a microbial culture comprising *Methylococcus capsulatus* (Bath), *Ralstonia sp*, *Brevibacillus agri* and *Aneurinibacillus sp* bacteria, does not reasonably provide enablement for a method of treating or preventing atherosclerosis or coronary heart disease comprising administering to an animal in need of such treatment, a pharmaceutical or nutritional composition comprising a single cell protein material, wherein the single cell protein material is harvested from a microbial culture comprising *Methylococcus* bacteria.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The facts that should be considered in determining whether a specification is enabling or if it would require an undue amount of experimentation to practice the invention include 1) the quantity of experimentation necessary to make or use the invention based on the content of the disclosure, (2) the amount of direction or guidance presented, 3) the presence or absence of

working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, the factors that weigh more in making the instant enablement rejection are discussed below.

Nature of the Invention/Breadth of the Claims

The invention is drawn to treatment or prevention of atherosclerosis or coronary heart disease in any type of animal comprising administering a composition (pharmaceutical or nutritional) comprising any type of single cell protein (SCP) material harvested from a microbial culture comprising *Methylococcus* bacteria.

Thus, the claims encompass treatment or prevention of atherosclerosis or coronary heart disease using SCP from any species of *Methylococcus* or using SCP from a culture that comprises any species of *Methylococcus* and other components including other microbial organisms such as fungi, yeasts and bacteria. Applicants' specification defines single cell protein material as a material comprising single cell microorganisms such as fungi, yeasts and bacteria. See page 9. The scope of the claims are very broad and the nature of the invention is highly complex because it involves the use of any type *SCP material* harvested from a culture

comprising any *Methylococcus* species or any *Methylococcus* species and any other type of microbe to treat or prevent a highly complex disease such as atherosclerosis or coronary heart disease. There are many *Methylococcus* species each species having different strains. Also there are many types of microbes each different from the other. In essence, the claims are partially drawn to using protein material as a "vaccine" to prevent atherosclerosis or coronary heart disease.

The scope of animals who would be in need of treatment or prevention of atherosclerosis or coronary heart disease includes those who are smokers, those who have diabetes mellitus, those who have hypertension and those who have hyperlipidemia or hypercholesterolemia. See previously cited articles by Canto et al. JAMA August 20, 2003 Vol. 290 p. 947-949, Link et al. West J. Med. 2002. 174: 330-5 and Domanski et al NEJM 357; 15, p. 1543-1545. Smoking, diabetes mellitus, hypertension and hyperlipidemia or hypercholesterolemia are conventional risk factors for developing heart disease.

The amount of direction or guidance presented and the presence or absence of working examples

The specifications teaching is limited to reducing plasma homocysteine, reducing triacylglycerols in the liver, reducing the activity of Acyl-CoA:cholesterol acyltransferase (ACAT), increasing mitochondrial β-oxidation and changing the fatty acyl profile in an experimental obese Zucker rat model comprising administering a pharmaceutical or nutritional composition comprising a particular single cell protein material harvested from a culture comprising a combination of microbes *Methylococcus capsulatus (Bath), Ralstonia sp, Brevibacillus agri and Aneurinibacillus sp*. See preparation of single cell material in example 1

p. 17 and various experimental results in animal model in examples 2-7. The specification does not administer SCP harvested from a culture consisting of Methylococcus and does not correlate treatment or prevention of atherosclerosis and coronary heart disease with SCP derived from a culture comprising only Methylococcus.

Even though the instant specification teaches that single cell protein material combination from *Methylococcus capsulatus(Bath), Ralstonia sp, Brevibacillus agri and Aneurinibacillus sp* lowers plasma cholesterol, lowers triacylglycerols in the liver, decreases the activity of Acyl-coA:cholesterol acyltransferase (ACAT) and increases mitochondrial beta-oxidation in obese Zucker rats, the specification does not correlate these results prevention or treatment of a highly complex diseases such as atherosclerosis or coronary heart disease. It is not clear whether the levels by which plasma cholesterol, triacylglycerols, activity of ACAT is reduced in the animal model is predictive of prevention of atherosclerosis or coronary heart disease in the animal model and in other animals e.g. humans.

The state of the prior art and the predictability or unpredictability of the art

The scope of animals who would be in need of treatment or prevention of atherosclerosis or coronary heart disease includes those who are smokers, those who have diabetes mellitus, those who have hypertension and those who have hyperlipidemia or hypercholesterolemia. See previously cited articles by Canto et al. JAMA August 20, 2003 Vol. 290 p. 947-949, Link et al. West J. Med. 2002. 174: 330-5 and Domanski et al NEJM 357; 15, p. 1543-1545. Smoking, diabetes mellitus, hypertension and hyperlipidemia or hypercholesterolemia are conventional risk factors for developing heart disease. It is not clear what role the instant SCP material plays in treating or preventing atherosclerosis or coronary heart disease in animals that have each of

these risk factors or a combination of one or more risk factors.

Canto et al teaches that atherosclerosis is a systemic disease in need of a systemic solution, and a comprehensive approach involving risk factor modification and pharmacological treatment is needed for effective prevention of cardiovascular disease (Canto et al p. 948 column 2 second to the last paragraph). Canto et al teaches that for patients with hypertension blood pressure should be controlled to less than 140/90mmHg in the overall population and to 130/80mmHg in those with diabetes or renal disease (Canto et al p. 948 column 2 second to the last paragraph). What role does the instant SCP material have in controlling hypertension or which is a risk factor for cardiovascular disease? Among patients with diabetes, tight control of blood glucose and hemoglobin A1c is important for prevention or treatment of cardiovascular disease (Canto et al p. 948 column 2 second to the last paragraph).What role does the instant SCP material have in maintaining tight control of blood glucose and hemoglobin A1c in patients with diabetes who are at risk for cardiovascular disease? Also in patients who smoke, does the instant SCP material treat or prevent cardiovascular disease in these patients. The answers to these questions are unpredictable because the examples in the specification are drawn to an animal model of hyperlipidemia (and hypercholesterolemia) (Vaskonen et al J. Nutr. 132:231-237, 2002, p. 231 column 2 second full paragraph) which is only one risk factor for development of atherosclerosis and coronary heart disease. Atherosclerosis and coronary heart disease are complex disease with multiple conventiontional risk factors such as smoking, diabetes mellitus, hypertension and hyperlipidemia and emerging risk factors such as C- reactive protein and other inflammatory markers (Canto et al .p. 948 column 1 last bridging paragraph).

The quantity of experimentation necessary to use the invention based on the content of

the disclosure

The specification has provided guidance as to reducing plasma homocysteine, reducing triacylglycerols in the liver, reducing the activity of Acyl-CoA:cholesterol acyltransferase (ACAT), increasing mitochondrial β-oxidation and changing the fatty acyl profile which are related to hyperlipidemia/hypercholesterolemia (one risk factor for coronary heart disease) in an experimental obese Zucker rat model comprising administering a pharmaceutical or nutritional composition comprising a particular single cell protein material harvested from a culture comprising a combination of microbes *Methylococcus capsulatus (Bath) , Ralstonia sp, Brevibacillus agri and Aneurinibacillus sp.*

The specification has *not* provided guidance as to reducing plasma homocysteine, reducing triacylglycerols in the liver, reducing the activity of Acyl-CoA:cholesterol acyltransferase (ACAT), increasing mitochondrial β-oxidation and changing the fatty acyl profile which are related to hyperlipidemia or hypercholesterolemia risk factors for coronary heart disease in an experimental obese Zucker rat model comprising administering a pharmaceutical or nutritional composition comprising a particular single cell protein material harvested from a culture comprising only *Methylococcus* i.e. any type of *Methylococcus*, or *Methylococcus* with any other type of fungi, bacteria or yeast.

Thus, a large quantity of experimentation would be required of the skilled artisan to screen SCP derived from different cultures containing each of the different *Methylocccus* species and their different strains for which one treats and prevents highly complex diseases such as atherosclerosis or coronary heart disease in all patients that have one or more combination of the risk factors listed above for atherosclerosis or coronary heart disease.

In conclusion, in view of the above considerations, undue experimentation would be required of the skilled artisan to use the instant invention commensurate with the full scope of the claims and the nature and breadth of the invention set forth above.

The specification, while being enabling for a method of reducing plasma homocysteine, reducing triacylglycerols in the liver, reducing the activity of Acyl-CoA:cholesterol acyltransferase (ACAT), increasing mitochondrial β-oxidation and changing the fatty acyl profile in an animal in need thereof comprising administering to said animal a pharmaceutical or nutritional composition comprising a single cell protein material, wherein the single cell protein material is harvested from a microbial culture comprising *Methylococcus capsulatus* (Bath), *Ralstonia sp*, *Brevibacillus agri* and *Aneurinibacillus sp* bacteria, does not reasonably provide enablement for a method of treating or preventing atherosclerosis or coronary heart disease comprising administering to an animal in need of such treatment, a pharmaceutical or nutritional composition comprising a single cell protein material, wherein the single cell protein material is harvested from a microbial culture comprising *Methylococcus* bacteria.

Status of Claim

Claims 22-23 and 44-50 are rejected. No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the

Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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